

NOTE: This article has been updated since print publication. In the original article, the Further Reading box (next page) incorrectly attributed the Pineles study to the Academy's Task Force on Myopia. It is actually attributable to the Academy Ophthalmic Technology Assessment Committee Pediatric Ophthalmology/Strabismus Panel. This version of the article corrects the mistake.

PEDIATRIC OPHTHALMOLOGY
CLINICAL UPDATE

Low-Dose Atropine to Slow Myopia: Evidence and Adoption Are Growing

The first studies about low-dose atropine to slow myopic progression in children were published about 20 years ago, eliciting a trickle of interest among pediatric ophthalmologists. As the worldwide prevalence of myopia grew to epidemic proportions, the influential Atropine for the Treatment of Myopia (ATOM1 and ATOM2) and LAMP (Low-Concentration Atropine for Myopia Progression) studies came out, and early adopting ophthalmologists started to integrate the drug into their practices. Then COVID hit, possibly pushing the myopia epidemic to new levels.¹

This confluence of factors has raised awareness of low-dose atropine for myopia not only among ophthalmologists but also among pediatricians, primary care physicians, and parents. Nonetheless, questions remain, even as scientific evidence and clinical experience among ophthalmologists accrue.

Analyzing the Research

The ATOM and LAMP studies in particular have been instrumental in capturing the attention of ophthalmologists. The ATOM1 study found atropine to be superior to placebo, and ATOM2 found that low dosages also slowed the progression of myopia. The LAMP study used a range of low dosages of atropine to see which was most effective.

In the wake of these major studies, research continues.

Age matters. Recently, a secondary analysis of LAMP data by Li et al. found that younger children require higher concentrations of the drug to achieve a benefit similar to older children on lower dosages. Specifically, the researchers stated that 6-year-old children who used 0.05% atropine had mean spherical equivalent progression similar to 8-year-olds on 0.025% atropine and 10-year-olds on 0.01% atropine.²

Diverse population.

K. David Epley, MD, a pediatric ophthalmologist in Kirkland, Washington, and an early adopter of low-dose atropine drops, joined with colleagues in a multicenter retrospective case review to assess the effectiveness of 0.01% atropine drops in a diverse group of pediatric patients in the United States.³

This review published in 2019 included myopic children of a variety of ethnicities aged 6-15 years. Controls were matched to study participants by age and spherical equivalent refraction. Patients were primarily Asian and White, with much smaller percentages of mixed-race children, Hawaii/Pacific Islanders, Blacks, and Native Americans. Study subjects received nightly atropine in addition to their typical eye care (e.g., single-vision eyeglasses or no glasses for low myopes). Controls



ATROPINE. Public awareness is growing about low-dose atropine for slowing myopia progression in children.

received only typical eye care.

After one year, atropine-treated patients had progressed by -0.2 ± 0.8 D, versus controls who progressed by -0.6 ± 0.4 D ($p < 0.001$). At two years, progression was -0.3 ± 1.1 D and -1.2 ± 0.7 D, respectively ($p < 0.001$). The authors concluded that atropine 0.01% could be safe and effective in reducing myopia progression in an ethnically diverse population.

Studies in progress. Currently, numerous studies are in progress, including ATOM3,⁴ a study at the Singapore National Eye Centre, which involves the use of low-dose atropine in children who are 5-9 years old either to prevent myopia in those whose parents are myopes or to slow progression in those with low myopia.

The Pediatric Eye Disease Investigator Group in collaboration with the NEI is studying the efficacy of 0.01% atropine in children aged 5-12 years in a sample that is no more than 25% East

BY KATHRYN MCKENZIE, CONTRIBUTING WRITER, INTERVIEWING K. DAVID EPLEY, MD, JENNIFER A. GALVIN, MD, FAAP, AND STACY L. PINELES, MD, MS.

Asian.⁵ It is studying the children over a treatment course of two years, and for six months after end of treatment.

And several prospective phase 3 trials are underway, such as Sydnexis's STAAR trial of its patented SYD-101,⁶ the Childhood Atropine for Myopia Progression (CHAMP) looking at Nevakar's NVK-002,⁷ and the CHALLENGE study of EyeNovia's Micropine novel dosing device.⁸ FDA approval of one or all of these products could make low-dose atropine more widely available, because at present, the drops can be obtained only from compounding pharmacies and are not typically covered by insurance, said Dr. Epley.

Putting Studies Into Practice

Ophthalmologists are finding that the 0.01% concentration is optimal as a starting dose, said Jennifer A. Galvin, MD, FAAP, at Yale School of Medicine in New Haven, Connecticut.

Starting dose. Dr. Galvin has been using 0.01% atropine eyedrops with her patients since 2014, based upon findings from ATOM2. She has treated some 60 patients between the ages of 6 and 13 years during this time. Citing observations from her practice, she said, "In the majority of my patients, especially the patients with strong family history of high myopia, there has been a stabilization and slowing of the myopic refractive error as well as the axial length measurement."

Stacy L. Pineles, MD, MS, also starts patients on this lowest dose. "I typically start with 0.01%, and if patients progress, I increase to 0.05%," she said, adding, "a lot of other physicians are starting with 0.05% based on LAMP." Dr. Pineles is at the University of California Stein Eye Institute in Los Angeles.

In fact, Dr. Galvin said that in summer 2020, based on results from LAMP, she increased the dosage for most of her patients from 0.01% to 0.05%. After she found that many patients had side effects of light sensitivity, she switched nearly all of them back to 0.01%.

For his part, Dr. Epley starts patients at 0.01% to avoid any unwanted side effects. "If the child's not stable or steady at 0.01%, I don't hesitate to move them up the scale a little bit. Combining atro-

pine in our practice with the new MiSight lenses from CooperVision and orthokeratology, I think we have a pretty effective protocol for slowing down myopia." (For more about MiSight, see "Beyond Atropine and Ortho-K: Contact Lenses for Mitigating Myopia Progression," *EyeNet*, February 2021 at aao.org/eyenet.)

Link to growth cycle. Dr. Epley said he now typically keeps younger children on the drops for five to seven years, usually to age 14. "If they're an older child and they started treatment at 11 or 12 years of age, then I'll usually stop them after five years," he said. He has observed among his own patients that those who start progressing at earlier ages are on the medication longer, since they have a lengthier growth cycle than youngsters whose myopia started to progress in the pre-teen or teen years.

Rebound effect. Dr. Epley noted the potential of a rebound effect when treatment is stopped. In his experience, the myopia is more likely to worsen if a patient has been on higher-concentration drops. "Over time, I have kept children on the drops longer to avoid this rebound effect, not stopping until the child is 14 to 15 years of age and less likely to continue to progress," he said.

Dilation observations. Dr. Epley has also noticed that lower doses are well tolerated with few side effects, which may increase as the percentage is bumped up. Even in White patients with light irides, who tend to have a little more pupil dilation than those with darker eyes, he noted that there are few problems. "At 0.05%, there's definitely a bit of blurring up close, which is tolerated by most kids. It's not so blurred that they can't do what they need to do," he said.

Unanswered questions. However, as treatment with low-dose atropine is relatively new and not FDA approved, questions remain.

Duration of treatment. Dr. Epley, who has treated about 190 patients with low-dose atropine since 2012, said he would like to see studies address how long to keep patients on the drops, and at what age to stop.

"It's clear that there are some kids who are done with their growth process

in terms of increasing myopia by the age of 12 or 13, and there are definitely a lot who are not," he said. "Initially, I was stopping kids at 13, which is what they did with the ATOM studies. And I found so many kids—a large percentage—who were not stable at that point, and their myopia would increase again."

Ethnicity. Dr. Pineles noted that some physicians are still hesitant to prescribe atropine because many of the larger studies thus far have involved only patients of Asian ethnicity. She said that she hopes more studies like that conducted by Dr. Epley and colleagues will address questions around ethnicity. And she looks forward to results from the PEDIG study.

Other questions. Dr. Pineles raised several additional questions: "First, what is the optimal age to start? Then, should we be waiting until the myopia rapidly progresses or trying to intervene even before that in high-risk families? And, when—and how—should we stop treatment?" She also noted that combination therapy is an important area for inquiry, for example combining low-dose atropine with multifocal lenses prescribed off-label, the latter of which was reported the BLINK study.⁹

Rising Awareness

Pediatricians, optometrists, and primary care physicians are referring patients specifically for this type of treatment, said Dr. Epley. Parents are also becoming more savvy; nearsighted parents

FURTHER READING

Pineles S et al. for the Academy's Ophthalmic Technology Assessment Committee Pediatric Ophthalmology/Strabismus Panel.

Atropine for the Prevention of Myopia Progression in Children. *Ophthalmology*. 2017;124:1857-1866.

Modjtahedi BS et al. for the Academy's Task Force on Myopia. **Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing Myopic Progression in Children.** *Ophthalmology*. 2021;128(6):816-826.



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are particularly concerned that their myopic children may follow in their footsteps, he said.

Dr. Pineles has also observed increased interest in low-dose atropine during the last year or two. “Given the low side-effect profile and the demonstrated efficacy in a disease that doesn’t have many other treatment options, families are asking for the drops, and physicians are recommending them.”

Finally, Drs. Epley, Galvin, and Pineles noted, getting the word out about low-dose atropine can be an enormous step forward in curbing the global myopia epidemic. “If we can reduce the number of kids who are -6 D or higher, over time, that will have a huge impact on eye health as they become adults,” said Dr. Epley. “So it’s worth doing. I’m eagerly awaiting the day that CHAMP and some of these other trials are finished so that we can get an FDA-approved product.”

1 Wang J et al. *JAMA Ophthalmol.* 2021;139(3):293-300.

2 Li FF et al. *Ophthalmology.* 2021;128(8):1180-1187.

3 Larkin GL et al. *Ophthalmol Ther.* 2019;8(4):589-598.

4 ATOM3. www.clinicaltrials.gov/ct2/show/NCT03140358.

5 PEDIG. www.clinicaltrials.gov/ct2/show/NCT03334253.

6 STAAR. www.clinicaltrials.gov/ct2/show/NCT03918915.

7 CHAMP. www.clinicaltrials.gov/ct2/show/NCT03350620.

8 EyeNovia. www.clinicaltrials.gov/ct2/show/NCT03942419.

9 Walline JJ et al. *JAMA.* 2020;324(6):571-580.

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Dr. Galvin is a principal investigator for the Pediatric Eye Disease Investigator Group at Eye Physicians & Surgeons PC and assistant clinical professor of ophthalmology and visual science at Yale School of Medicine in New Haven, Conn. *Financial disclosures: None.*

Dr. Pineles is associate professor of ophthalmology and residency program director at the Stein Eye Institute, University of California, Los Angeles. *Financial disclosures: None.*

See disclosure key, page 10.